09/277,074 Davis

=> fil hcaplu

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23 SEA FILE=REGISTRY KIFGSLAFL/SQSP L1

L2 39 SEA FILE=HCAPLUS L1

360 SEA FILE=REGISTRY T (5A) LYMPHOCYTE? L3

119631 SEA FILE=HCAPLUS L3 OR T(5A)(CELL? OR LYMPHOCYTE?) L4

24 SEA FILE=HCAPLUS L4 AND L2 **T.5**

=> d ibib abs hitrn 15 1-24

ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 2000:645832 HCAPLUS

133:256752 DOCUMENT NUMBER:

Microparticles for delivery of nucleic acid TITLE:

Lunsford, Lynn B.; Putnam, David; Hedley, Mary Lynne INVENTOR(S):

Zycos Inc., USA PATENT ASSIGNEE(S):

PCT Int. Appl., 96 pp. SOURCE:

CODEN: PIXXD2

Patent DOCUMENT TYPE:

English LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. _____ ____ _____ WO 2000-US6578 20000914 20000310 A2 WO 2000053161

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W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
             IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                           US 1999-266463
                                                            19990311
                                           US 1999-321346
                                                            19990527
     A prepn. of microparticles made up of a polymeric matrix, a nucleic acid
AB
     expression vector, and a lipid is disclosed. The polymeric matrix
     includes one or more synthetic polymers having a soly. in water of less
     than about 1 mg/L. At least 90 % of the microparticles have a diam. less
     than about 100 .mu.. The nucleic acid is either RNA, at least 50 % of
     which is in the form of closed circles, or circular DNA plasmid mols., at
     least 50 % of which are supercoiled.
     160212-35-1
TΤ
     RL: PRP (Properties)
        (unclaimed sequence; microparticles for delivery of nucleic acid)
     ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2000 ACS
                         2000:592741 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         133:191988
TITLE:
                         Protein preparations
                         Shinbara, Naoki; Udono, Heiichiro; Yui, Katsuyuki
INVENTOR(S):
                         Sumitomo Electric Industries, Ltd., Japan
PATENT ASSIGNEE(S):
SOURCE:
                         PCT Int. Appl., 72 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         Japanese
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                     KIND
                            DATE
                                           APPLICATION NO.
                                                            DATE
     _____
     WO 2000049041
                      A1
                            20000824
                                           WO 2000-JP941
                                                            20000218
         W: JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE PRIORITY APPLN. INFO.:
                                           JP 1999-41535
                                                            19990219
AB
     A fused protein which is capable of inducing a potent cellular immune
     response and thus useful in treating or preventing infectious diseases
     such as malaria or diseases such as cancer; and medicinal compns. contg.
     this fused protein as the active ingredient. Namely, a fused protein
     composed of a peptide contg. a CTL epitope recognized by cytotoxic
     T cells and a protein contq. the ATPase domain of heat
     shock protein; medicinal compns. contg. this fused protein as the active
     ingredient; a DNA encoding the fused protein; an expression vector contq.
     this DNA; and a transformant carrying this expression vector. The most
     efficacious way for administering the medicinal compns. is i.v. injection
     into a living body.
```

IT 160212-35-1

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cytotoxic T lymphocyte epitope; heat shock proteins or fusion proteins for treating and preventing infectious diseases such as malaria and cancers) REFERENCE COUNT: REFERENCE(S): (1) Kimiko, S; Proc Natl Acad Sci USA 1997, V94, P13146 (2) Minka, B; European Journal of Immunology 1998, V28(3), P1016 (3) Nathalie, E; J Exp Med 1997, V186(8), P1315 (4) Tatsuaki, I; The Journal of Immunology 1999, V162(3), P1303 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 2000:402017 HCAPLUS DOCUMENT NUMBER: 133:54574 TITLE: Recombinant vectors expressing multiple costimulatory molecules, host cell infection, and uses in immunogenic applications INVENTOR(S): Schlom, Jeffrey; Hodge, James; Panicali, Dennis PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Therion Biologics Corporation PCT Int. Appl., 188 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE _____ ____ _____ -----20000615 WO 1999-US26866 19991112 WO 2000034494 A1 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.: US 1998-111582 19981209 AB The present invention provides recombinant vectors encoding and expressing at least three or more costimulatory mols and host cells infected by the vector. The recombinant vector may addnl. contain a gene encoding one or more target antigens or immunol. epitope as well as cytokine, chemokine, or Flt-3L. A method of making a recombinant poxvirus, of enhancing an immune response of an individual by administering a recombinant vector, and of treating or preventing a disease by activating a T lymphocyte, are also presented. Further describes are a method of making a progenitor dendritic cell or dendritic cell, of assesing the efficacy of a vaccine against a target antigen, and of screening for novel immunogenic peptides. The synergistic effect of these costimulatory mols.

recombinant vectors contg. genes encoding three costimulatory mols. was far greater than the sum of recombinant vector constructs contg. one

on the enhanced activation of T cells was

demonstrated. The degree of T-cell activation using

```
costimulatory mol. and greater than the use of two costimulatory mols.
     Results employing the triple costimulatory vectors were most dramatic
     under conditions of either low levels of first signal or low stimulator to
     T-cell ratios. This phenomenon was obsd. with both
     isolated CD4+ and CD8+ T cells. The recombinant
     vectors of the present invention are useful as immunogenes and vaccines
     against cancer and pathogenic micro-organisms, and in providing host
     cells, including dendritic cells and splenocytes with enhanced
     antigen-presenting functions.
     160212-35-1
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
        (amino acid sequence; Recombinant vectors expressing multiple
        costimulatory mols., host cell infection, and uses in immunogenic
        applications)
REFERENCE(S):
```

REFERENCE COUNT:

ΙT

(1) Hodge, J; Cancer Res 1999, V59, P5800 HCAPLUS

(2) Keting, C; US 5738852 A 1998 HCAPLUS (3) Therion Biolog Corp; WO 9804727 A 1998

(4) US Health; WO 9610419 A 1996

ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 2000:240985 HCAPLUS

DOCUMENT NUMBER: 132:292701

TITLE: Novel methods for therapeutic vaccination

Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla M Amp E Biotech A/s, Den. INVENTOR(S):

PATENT ASSIGNEE(S): PCT Int. Appl., 220 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	PATENT NO.					DATE			A	PPLI	CATI	٥.	DATE						
									_										
WO	2000	2000020027			2	20000413			W	0 19	99-D	K525		19991005					
WO	2000	020027		A3		20001012													
	w:	W: AE, AL, CU, CZ, GH, GM, LR, LS, RU, SD,		AM,	ΑT,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,		
				CZ,	DE,	DE,	DK,	DK,	DM,	EE,	EE,	ES,	FI,	FI,	GB,	GD,	GE,		
				HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,		
				LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,		
				SE,	SG,	SI,	SK,	SK,	SL,	ТJ,	TM,	TR,	TT,	UΑ,	ŪĠ,	US,	UZ,		
		VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM					
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	ΑT,	BE,	CH,	CY,	DE,		
		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,		
		CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG						
PRIORITY	APP	LN.	INFO	. :					D	K 19	98-1	261		19981005					
									US 1998-105011 19981020										

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the

weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.

IT 264179-59-1, Neu (receptor) (human)

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(amino acid sequence; weak antigens inserted with foreign **T** cell epitope as vaccines)

IT 264622-09-5, Human Her2 protein (369-383)

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(weak antigens inserted with foreign T cell epitope as vaccines)

L5 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:98610 HCAPLUS

DOCUMENT NUMBER:

132:165123

TITLE:

Heterominibodies

INVENTOR(S):

Kufer, Peter; Dreier, Torsten; Baeuerle, Patrick A.;

Borschert, Katrin; Zettl, Florian

PATENT ASSIGNEE(S):

Micromet Gesellschaft Fur Biomedizinische Forschung

m.b.H., Germany

SOURCE:

PCT Int. Appl., 166 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.					ND	DATE			A	PPLI	CATI	ON N	ο.	DATE					
	WO	2000006605			A	A2 20000210			WO 1999-EP5416						19990728					
	WO	2000	0660	5	A 3		20000629													
		W:	ΑE,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,		
			DE,	DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,		
			JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,		
		MN, MW, TM, TR,		ΜX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	sĸ,	SL,	TJ,			
				TT,	UA,	ŪĠ,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	KZ,			
			MD,	RU,	ТJ,	TM														
		RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,		
			ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,		
			CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG							
	AU 9957289					A1 20000221				A	J 19:	99~5	7289		19990728					
PRIO	RIORITY APPLN. INFO.					.:				EP 1998-114082					19980728					
										W	19	99-E	P541	6	19990728					
7 D	m\.			2			- 1 - 4			7		_4_2	7							

AB The present invention relates to a multifunctional compd., produceable in a mammalian host cell as a secretable and fully functional heterodimer of two polypeptide chains, wherein one of said polypeptide chains comprises, as the only const. region domain of an Ig heavy chain the CH1-domain and

the other polypeptide chain comprises the const. CL-domain of an Ig light chain, wherein said polypeptide chains further comprise, fused to said const. region domains at least two (poly)peptides having different receptor or ligand functions, wherein further at least two of said different (poly)peptides lack an intrinsic affinity for one another and wherein said polypeptide chains are linked via said const. domains. Preferably, said domains, having receptor or ligand function, are in the format of a scFv-fragment and/or are immuno-modulating effector mols. Most preferably, said scFV-fragment comprises the VH and the VL regions of the murine anti-17-1A antibody M79, the VH and the VL regions of the anti-Lewis Y antibody, as shown in Fig. 6, or the VH and the VL regions of the anti-CD3 antibody TR66 and/or said immuno-modulating effector mol. comprises cytokines or chemokines. Furthermore, the present invention relates to polynucleotides encoding said polypeptide chains as well as vectors comprising said polynucleotides and host cells transformed therewith as well as the use of the above embodiments for the prodn. of said multifunctional compds. In addn., pharmaceutical and diagnostic compns. are provided, comprising any of the afore-described multifunctional compds., polynucleotides or vectors. Described is also the use of the afore-mentioned multifunctional compd. for preventing and/or treating malignant cell growth, related to malignancies of hemopoietic cells or to solid tumors. Thus, heterominibody comprising (1) scFv of murine anti-17-1A antibody M79 and human CD80 extracellular domain, (2) scFv of anti-Lewis Y and CD80 extracellular domain, (3) M79scFv and CD54, (4) M79scFv and CD58, (5) M79scFv and CD86, (6) M79scFv and anti-CD3 scFv and CD80, (7) anti-EpCAM (HD70scFv) linked to GM-CSF and anti-EpCAM (HD70scFv) linked to interleukin 2 were prepd. and tested. 258494-99-4

IT 258494-99-4 RL: PRP (Properties)

SOURCE:

PUBLISHER:

(amino acid sequence; heterominibodies for preventing and treating malignancies of hemopoietic cells and solid tumors)

L5 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:2207 HCAPLUS

DOCUMENT NUMBER: 132:106652

TITLE: Poor binding of a HER-2/neu epitope (GP2) to HLA-A2.1

is due to a lack of interactions with the center of

the peptide

AUTHOR(S): Kuhns, Jennifer J.; Batalia, Michael A.; Yan, Shuqin;

Collins, Edward J.

CORPORATE SOURCE: Department of Microbiology and Immunology, University

of North Carolina, Chapel Hill, NC, 27599, USA

J. Biol. Chem. (1999), 274(51), 36422-36427

CODEN: JBCHA3; ISSN: 0021-9258

American Society for Biochemistry and Molecular

Biology

DOCUMENT TYPE: Journal LANGUAGE: English

AB Class I major histocompatibility complex (MHC) mols. bind short peptides derived from proteins synthesized within the cell. These complexes of peptide and class I MHC (pMHC) are transported from the endoplasmic reticulum to the cell surface. If a clonotypic T cell receptor expressed on a circulating T cell binds to the pMHC complex, the cell presenting the pMHC is killed. In this manner, some tumor cells expressing aberrant proteins are recognized and removed by the immune system. However, not all tumors are recognized efficiently.

One reason hypothesized for poor T cell recognition of tumor-assocd. peptides is poor binding of those peptides to class I MHC mols. Many peptides, derived from the proto-oncogene HER-2/neu have been shown to be recognized by cytotoxic T cells derived from HLA-A2+ patients with breast cancer and other adenocarcinomas. Seven of these peptides were found to bind with intermediate to poor affinity. In particular, GP2 (HER-2/neu residues 654-662) binds very poorly even though it is predicted to bind well based upon the presence of the correct HLA-A2.1 peptide-binding motif. Altering the anchor residues to those most favored by HLA-A2.1 did not significantly improve binding affinity. The crystallog. structure shows that unlike other class I-peptide structures, the center of the peptide does not assume one specific conformation and does not make stabilizing contacts with the peptide-binding cleft.

IT 160212-35-1P

> RL: BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (poor binding of a HER-2/neu epitope (GP2) to HLA-A2.1 due to lack of interactions with the center of the peptide)

REFERENCE COUNT:

39

REFERENCE(S):

- (1) Adams, P; Proc Natl Acad Sci 1997, V94, P5018 **HCAPLUS**
- (3) Batalia, M; Biopoly 1997, V43, P281 HCAPLUS
- (4) Bouvier, M; Science 1994, V265, P398 HCAPLUS
- (7) Chan, S; Immunol Rev 1998, V165, P195 HCAPLUS
- (8) Chen, Y; J Immunol 1994, V152, P2874 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER:

1999:740217 HCAPLUS

DOCUMENT NUMBER:

132:221298

TITLE:

HER-2/neu peptide specificity in the recognition of

HLA-A2 by natural killer cells

AUTHOR (S):

Anderson, Larry D., Jr.; Hudson, J. Michael; Savary, Cherylyn A.; Fisk, Bryan; Gershenson, David M.;

Ioannides, Constantin G.

CORPORATE SOURCE:

Department of Gynecologic Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030,

SOURCE:

Cancer Immunol. Immunother. (1999), 48(7), 401-410

CODEN: CIIMDN; ISSN: 0340-7004

PUBLISHER:

Springer-Verlag

DOCUMENT TYPE:

Journal English

LANGUAGE:

Although natural killer (NK) cells have been described as AB non-MHC-restricted, new evidence suggests that NK activity can be either up- or down-regulated after interaction with the peptide-MHC class-I complex expressed on target cells. However, the epitope(s) recognized by NK cells have remained ill-defined. The authors investigated NK cell recognition of synthetic peptides representing a portion of a self-protein encoded by the HER-2/neu (HER-2) proto-oncogene and presented by HLA-A2. HER-2 nonapeptides C85, E89, and E75 were found partially to protect T2 targets from lysis by freshly isolated and interleukin-2 (IL-2)-activated NK cells (either HLA-A2+ or A2-). This inhibition was not solely due to changes in the level of HLA-A2 expression or conformation of serol. HLA-A2 epitopes. Using single-amino-acid variants at position 1 (P1) of two

HER-2 peptides, the authors obsd. that protection of targets was dependent on the sequence and the side-chain. These results suggest similarities in the mechanism of target recognition by NK and **T cells**. This information may be important for understanding the mechanisms of tumor escape from immunosurveillance and could help explain the aggressiveness of HER-2-overexpressing tumor cells.

IT 160212-35-1

RL: PRP (Properties)

(HER-2/new peptide specificity in recognition of HLA-A2 by natural

killer cells)

REFERENCE COUNT: 42

REFERENCE(S): (1) Borrego, F; J Exp Med 1998, V187, P813 HCAPLUS

(2) Bouvier, M; Science 1994, V265, P398 HCAPLUS

(3) Brooks, A; J Immunol 1999, V162, P305 HCAPLUS

(4) Brutkiewicz, R; J Virol 1995, V69, P3967 HCAPLUS

(5) Catipovic, B; J Exp Med 1992, V176, P1611 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1999:677539 HCAPLUS

DOCUMENT NUMBER: 132:48743

TITLE: H-2 class I knockout, HLA-A2.1-transgenic mice. A

versatile animal model for preclinical evaluation of

antitumor immunotherapeutic strategies

AUTHOR(S): Firat, Huseyin; Garcia-Pons, Francisco; Tourdot,

Sophie; Pascolo, Steve; Scardino, Antonio; Garcia, Zacarias; Michel, Marie-Louise; Jack, Ralph Wiliams; Jung, Gunther; Kosmatopoulos, Konstadinos; Mateo, Luis; Suhrbier, Andreas; Lemonnier, Francois A.;

Langlade-Demoyen, Pierre

CORPORATE SOURCE: Unite Immunite Cellulaire Antivirale, Dep.

SIDA-Retrovirus, Institut Pasteur, Paris, F-75724, Fr.

SOURCE: Eur. J. Immunol. (1999), 29(10), 3112-3121

CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal LANGUAGE: English

AB H-2 class I-neg., HLA-A2.1-transgenic HHD mice were used for a comparative

evaluation of the immunogenicity of HLA-A2.1-restricted human

tumor-assocd. cytotoxic T lymphocyte (CTL) epitopes.

A hierarchy was established among these peptides injected into mice in incomplete Freund's adjuvant which correlates globally with their capacity to bind and stabilize HLA-A2.1 mols. Co-injection of a helper peptide enhanced most CTL responses. In contrast, classical HLA class I-transgenic mice which still express their own class I mols. did not, in most cases, develop HLA-A2.1-restricted CTL responses under the same exptl. conditions. Different monoepitope immunization strategies of acceptable clin. usage were compared in HHD mice. Recombinant Ty-virus-like particles, or DNA encoding epitopes fused to the hepatitis B virus middle envelope protein gave the best results. Using this latter approach and a melanoma-based polyepitope construct, CTL responses against 5 distinct epitopes could be elicited simultaneously in a single animal. Thus, HHD mice provide a versatile animal model for preclin. evaluation of peptide-based cancer immunotherapy.

IT 160212-35-1

RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);

BIOL (Biological study); PROC (Process); USES (Uses)

(preclin. evaluation of peptide-based cancer immunotherapy using

HLA-A2.1-restricted tumor-assocd. CTL epitopes)

REFERENCE COUNT: 32

REFERENCE(S): (1) Arnold, B; Annu Rev Immunol 1991, V9, P297 HCAPLUS

(3) Burns, N; Mol Biotechnol 1994, V1, P137 HCAPLUS

(4) Deres, K; Nature 1989, V342, P561 HCAPLUS

(5) Falk, K; Nature 1991, V351, P290 HCAPLUS (6) Gao, G; Nature 1997, V387, P630 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2000 ACS

1998:728119 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 130:94160

Immunization with a peptide epitope (p369-377) from TITLE:

HER-2/neu leads to peptide-specific cytotoxic

T lymphocytes that fail to recognize

HER-2/neu+ tumors

Zaks, Tal Z.; Rosenberg, Steven A. AUTHOR(S):

CORPORATE SOURCE: Surgery Branch, National Cancer Institute, NIH,

Bethesda, MD, 20892-1502, USA

SOURCE: Cancer Res. (1998), 58(21), 4902-4908

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: AACR Subscription Office

DOCUMENT TYPE: Journal

LANGUAGE: English

The oncogene HER-2/neu is genetically amplified and overexpressed in a large no. of human adenocarcinomas and has been implicated in the tumorigenic phenotype. Although it is a non-mutated self-protein, it is barely detectable in adult tissues, and immune responses toward it have been described in a no. of patients. It is, thus, an attractive candidate antigen for the immunotherapy of cancer patients. HLA-A2+ patients with metastatic breast, ovarian, or colorectal adenocarcinomas that over-expressed HER-2/neu were immunized with the HLA-A2-binding epitope p369-377 (p369). Patients were treated by repeated immunization with 1 mg of p369 in Freund's incomplete adjuvant every 3 wk. Peripheral blood mononuclear cells were collected prior to immunization and following two and four immunizations and were stimulated in vitro with peptide and assayed for peptide and tumor recognition. In three of four patients, peptide-specific CTLs were detected in post- but not pre-immunization These CTLs recognized peptide-pulsed target cells at peptide concns. of .gtoreq.1 ng/mL yet failed to react with a panel of HLA-A2+ HER-2/neu+ tumor lines. In addn., infecting HLA-A2+ cells with recombinant vaccinia virus encoding HER-2/neu or up-regulating HLA-A2 with IFN-.gamma. in HER-2/neu+ cells also failed to confer reactivity by p369-reactive T-cells. A T-cell

response to the HLA-A2 binding epitope p369 can be easily generated by immunizing patients with peptide in Freund's incomplete adjuvant. However, the CTLs failed to react with HER-2/neu+ tumor cells. Further studies are needed to det. whether and how HER-2 might serve as an antigen for tumor immunotherapy.

TΤ 160212-35-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (peptide epitope from HER-2/neu induces human peptide-specific cytotoxic T-cells that fail to recognize HER-2/neu-pos. tumors)

REFERENCE COUNT:

REFERENCE(S):

- (1) Abrams, S; Eur J Immunol 1996, V26, P435 HCAPLUS
- (2) Bargmann, C; Nature (Lond) 1986, V319, P226 **HCAPLUS**
- (3) Benz, C; Breast Cancer Res Treat 1993, V24, P85 HCAPLUS
- (4) Brossart, P; Cancer Res 1998, V58, P732 HCAPLUS
- (6) Coussens, L; Science (Washington DC) 1985, V230, P1132 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER:

1998:642619 HCAPLUS

DOCUMENT NUMBER:

130:64884

TITLE:

Identification of HER2/neu-derived peptide epitopes

recognized by gastric cancer-specific cytotoxic

T lymphocytes

AUTHOR (S):

Kono, Koji; Rongcun, Yang; Charo, Jehad; Ichihara, Fumiko; Celis, Esteban; Sette, Alessandro; Appella, Ettore; Sekikawa, Takayoshi; Matsumoto, Yoshiro;

Kiessling, Rolf

CORPORATE SOURCE:

First Department of Surgery, Yamanashi Medical

SOURCE:

AΒ

University, Yanmanashi, Japan Int. J. Cancer (1998), 78(2), 202-208 CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER:

Wiley-Liss, Inc.

DOCUMENT TYPE:

Journal English

LANGUAGE:

We have derived HLA-A2.1-restricted, gastric cancer-specific cytotoxic T lymphocyte (CTL) lines by repetitive in vitro stimulation of tumor-assocd. lymphocytes (TAL) with autologous tumor cells. The HER2/neu specificity of these gastric cancer-specific CTLs was demonstrated using HER2/neu-transfected cell lines and HER2/neu-expressing tumors, and with a set of HER2/neu-derived peptide epitopes. Gastric cancer-specific CTLs specifically lysed autologous and allogeneic HLA-A2.1+, HER2/neu+ gastric cancer cells, HER2/neu-transfected CIR/A2 cell lines (HLA-A2.1+, HER2+) and HLA-A2.1-transfected SW626 tumor cell lines (HLA-A2.1+, HER2+). This recognition could be inhibited by anti-HLA-A2 antibody or by cold target HER2/neu-transfected CIR/A2 cells. Our results demonstrate that the HER2/neu-encoded HLA-A2.1-assocd. epitopes recognized by CTLs are presented as naturally processed peptides on gastric cancer lines. Furthermore, 3 of 19 tested HER2/neu-derived peptide epitopes [HER2(9106), HER2(9369), HER2(9689)], which all bound HLA-A2.1 with high (IC50 < 50 nM) affinity, were able to sensitize HLA-A2+ CIR/A2 cells to be recognized by the gastric cancer-specific CTLs, demonstrating the immunodominance of these epitopes. In conclusion, our findings implicate HER2/neu-derived epitopes as potential candidates for novel immunotherapy and vaccine strategies against gastric cancer.

IT 160212-35-1

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(identification of HER2/neu-derived peptide epitopes recognized by ${\tt HLA-A2.1-restricted}$ gastric cancer-specific cytotoxic ${\tt T}$

lymphocytes)

REFERENCE COUNT:

REFERENCE(S):

(1) Coussens, L; Science 1985, V230, P1132 HCAPLUS

(2) Cox, A; Science 1994, V264, P716 HCAPLUS

```
(4) Fisk, B; J exp Med 1995, V181, P2109 HCAPLUS
                             (5) Hoshino, T; Int J Cancer 1997, V70, P631 HCAPLUS
                             (6) Ikeda, H; Cancer Res 1993, V53, P3078 HCAPLUS
                            ALL CITATIONS AVAILABLE IN THE RE FORMAT
L5
     ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2000 ACS
                            1998:543146 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                            129:160626
TITLE:
                            Peptides and peptide-loaded antigen presenting cells
                            for the activation of CTL
INVENTOR(S):
                            Tsai, Van; Southwood, Scott; Sidney, John; Sette,
                            Alessandro; Celis, Esteban
PATENT ASSIGNEE(S):
                            Epimmune, Inc., USA
SOURCE:
                            PCT Int. Appl., 104 pp.
                            CODEN: PIXXD2
DOCUMENT TYPE:
                            Patent
LANGUAGE:
                            English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                                          APPLICATION NO. DATE
                   KIND DATE
                        ----
                                                -----
     WO 9833888 Al 19980806 WO 1998-US1959 19980130
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
          NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
              GA, GN, ML, MR, NE, SN, TD, TG
                  A1 19980825
A1 20000628
                                           AU 1998-61409
EP 1998-906086
     AU 9861409
                                                                    19980130
     EP 1012238
                                                                    19980130
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
PRIORITY APPLN. INFO.:
                                                US 1997-36696
                                                                    19970131
                                                WO 1998-US1959
                                                                   19980130
     The authors disclose methods for generating antigen-specific cytotoxic
AB
     T lymphocytes (CTLs) in vitro. Antigen presenting cells
     (APCs), preferably dendritic cells, are pretreated with growth factors
     (e.g., GM-CSF and IL-4), loaded with antigenic peptide, and cultured with
     CTL precursors. Interleukin-7 is generally added at day 1 of the
     incubation; IL-10 generally added one day later and during restimulation.
     The activated cytotoxic T-cells so obtained may be
     used for adoptive therapy of cancer and infection. The invention also
     comprises methods for using peptide pulsed dendritic cells to identify
     novel MHC class I-restricted tumor antigens and subdominant epitopes.
IT
     160212-35-1
     RL: BAC (Biological activity or effector, except adverse); PRP
     (Properties); BIOL (Biological study)
         (peptide epitope identification and peptide-loaded antigen presenting
      cells for activation of cytotoxic T-cells)
```

ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2000 ACS

1998:506357 HCAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER: 129:229561

TITLE: Growth and antigen recognition of tumor-infiltrating

lymphocytes from human breast cancer

AUTHOR(S): Hudson, J. Michael; Castilleja, Agapito; Murray, James

L.; Honda, Toshie; Kudelka, Andrezj; Singletary, Eva;

Wharton, J. Taylor; Ioannides, Constantin G.

CORPORATE SOURCE: Dep. Gynecologic Oncology, Anderson Cancer Center,

Houston, TX, 77030, USA

SOURCE: J. Interferon Cytokine Res. (1998), 18(7), 529-536

CODEN: JICRFJ; ISSN: 1079-9907

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

In the present study, the authors isolated tumor-infiltrating lymphocytes (TIL) from 21 primary solid tumors and tumor-assocd. lymphocytes (TAL) from 9 malignant effusions, resp., of breast cancer patients. Significant proliferation and expansion of T cells was obsd. in 23 of 30 distinct samples. The TIL cultures were initiated using OKT3 mAb in the presence of moderate concns. (25-50 U/mL) of IL-2, followed by 100 U/mL of tumor necrosis factor (TNF)-.alpha.. TAL were not stimulated with OKT3 mAb, but all were successfully expanded in culture in the presence of IL-2 alone or together with TNF-.alpha.. Seven of nine distinct TAL grew in culture as predominantly CD4+ lines. In contrast, only 14 of 21 (66%) of primary breast TIL expanded in culture and were predominantly of CD8+ phenotype. Autologous tumor lysis was obsd. in seven of eight cases tested. Only one of the four TIL tested and one of the four TAL tested preferentially lysed autologous tumor. HER-2 peptide E75 (369-377) was recognized by two TIL lines of the five primary TIL tested and three of the for TAL tested. This suggests that E75 may be recognized by primary breast tumors. This may be of interest in developing vaccine strategies for therapeutic management of breast cancer.

IT 160212-35-1

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(expansion and antigen recognition of tumor-infiltrating lymphocytes from human breast cancer)

L5 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:178119 HCAPLUS

DOCUMENT NUMBER: 128:213387

TITLE: Immune reactivity to HER-2/neu protein for diagnosis

and treatment of malignancies in which the HER-2/neu

oncogene is associated

INVENTOR(S): Cheever, Martin A.; Disis, Mary L.

PATENT ASSIGNEE(S): University of Washington, USA

SOURCE: U.S., 54 pp. Cont. of U.S. Ser. No. 414,417.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5726023	A	19980310	US 1995-467083	19950606
US 5801005	Α	19980901	US 1995-414417	19950331

US 1993-33644 19930317 US 1993-106112 19930812 US 1995-414417 19950331

Methods for the detection, monitoring and treatment of malignancies in AB which the HER-2/neu oncogene is assocd, are disclosed. CD4+ T cells and antibodies responsive to p185HER-2/neu protein and peptides can be detected in higher frequency in patients with breast cancer than normal individuals. Detection of specific T cell activation (e.g., by measuring the proliferation of ${f T}$ cells) in response to in vitro exposure to the HER-2/new protein, or detection of immunocomplexes formed between the HER-2/neu protein and antibodies in body fluid, allows the diagnosis of the presence of a malignancy in which the HER-2/neu oncogene is assocd. Antibodies (e.g., c-neu Ab-3) used for detecting the HER-2/neu protein immunoblotting are derived by immunization of BALB/c mice with the peptide TAENPEYLGLDVPV, from the C-terminal domain of human c-neu protein, and fusion of mouse splenocytes with SP2/0 myeloma cells. The present invention also discloses methods and compns., including peptides, for treating such malignancies. Thus, CD4+ or CD8+ T cells are stimulated to proliferate in the presence of HER-2/neu protein or its peptide fragments, and then the proliferated T cells are administered to the animal in an ED. Peptide-based vaccines elicit immunity to HER-2/neu.

IT 100630-38-4, Receptor (human MKN-7 cell gene c-erbB2 precursor
 protein moiety reduced)

RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(immune reactivity to HER-2/neu protein for diagnosis and treatment of malignancies in which the HER-2/neu oncogene is assocd.)

IT 204380-34-7

PRIORITY APPLN. INFO.:

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (new peptides specific for CD4-pos. **T cell** activation; immune reactivity to HER-2/new protein for diagnosis and treatment of malignancies in which the HER-2/new oncogene is assocd.)

IT 160212-35-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (new peptides specific for CD8-pos. T cell activation; immune reactivity to HER-2/new protein for diagnosis and treatment of malignancies in which the HER-2/new oncogene is assocd.)

L5 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER:

1998:122486 HCAPLUS

DOCUMENT NUMBER:

128:242733

TITLE:

Her-2/neu-derived peptides are tumor-associated antigens expressed by human renal cell and colon

carcinoma lines and are recognized by in vitro induced

specific cytotoxic T lymphocytes

AUTHOR(S):

Brossart, Peter; Stuhler, Gernot; Flad, Thomas; Stevanovic, Stefan; Rammensee, Hans-Georg; Kanz,

Lothar; Brugger, Wolfram

CORPORATE SOURCE:

Department of Hematology, Oncology and Immunology, University of Tubingen, Tubingen, D-72076, Germany

SOURCE:

Cancer Res. (1998), 58(4), 732-736

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER:

American Association for Cancer Research

DOCUMENT TYPE:

Journal

LANGUAGE: English

The Her-2/neu oncogene encodes a Mr 185,000 transmembrane protein with homol. to the epidermal growth factor receptor. It is overexpressed in 30-40% of breast and ovarian cancers, and this overexpression was shown to correlate with aggressiveness of malignancy and poor prognosis. Using tumor-assocd. lymphocytes isolated from patients with ovarian or breast cancer, several HLA-A2-restricted, Her-2/neu-derived peptides were identified. Further studies revealed that these tumor-assocd. CTLs can also lyse other tumors, including non-small cell lung and pancreatic cancer cells, suggesting that Her-2/neu epitopes are shared between several distinct types of epithelial tumors. To analyze whether Her-2/neu epitopes are tumor-assocd. antigens for renal cell carcinoma (RCC) and colon carcinoma, we induced Her-2/neu peptide-specific CTL responses by primary in vitro immunization and used these CTLs to det. the presentation of Her-2/neu epitopes on human tumor lines. Autologous dendritic cells (DCs) generated from peripheral blood monocytes were pulsed with Her-2/neu-derived peptides E75 and GP2 and used as antigen-presenting cells for CTL priming. High CTL activity toward peptide-pulsed targets was obtained after two weekly restimulations. CTLs induced with DCs generated in the presence of TNF-.alpha. elicited a higher cytotoxic activity when they were stimulated with the cognate peptide than did CTLs induced with DCs grown in granulocyte macrophage colony-stimulating factor and interleukin 4 alone. The cytotoxicity of induced CTLs was antigen specific and HLA-A2 restricted. Furthermore, these CTLs lysed, in a MHCand antigen-restricted fashion, not only breast cancer cells but also colon carcinoma and RCC cell lines expressing Her-2/neu. The cytotoxic activity against tumor cells was blocked by cold HLA-A2-pos. targets pulsed with the cognate peptide in cold target inhibition assay and by anti-HLA-A2 monoclonal Ab. These results suggest that epitopes derived from Her-2/neu protein might be attractive candidates for broadly applicable vaccines and may prove useful for adoptive immunotherapies designed for colon carcinoma or RCC.

TΨ 160212-35-1

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Her-2/neu-derived peptides are tumor-assocd. antigens expressed by human renal cell and colon carcinoma lines and are recognized by in vitro induced specific cytotoxic T lymphocytes)

ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2000 ACS

1997:693545 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 128:2716

TITLE: Generation and phenotypic characterization of new

human ovarian cancer cell lines with the

identification of antigens potentially recognizable by

HLA-restricted cytotoxic T cells

Ramakrishna, Venkatesh; Negri, Donatella R. M.; AUTHOR (S):

Brusic, Vladimir; Fontanelli, Rosanna; Canevari, Silvana; Bolis, Giorgio; Castelli, Chiara; Parmiani,

Giorgio

Division of Experimental Oncology D, Istituto CORPORATE SOURCE:

Nazionale Tumori, Milan, Italy

SOURCE: Int. J. Cancer (1997), 73(1), 143-150

CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal LANGUAGE: English

This study describes a simple method for long-term establishment of human ovarian tumor lines and prediction of T-cell epitopes that could be potentially useful in the generation of tumor-specific cytotoxic T lymphocytes (CTLs). Nine ovarian tumor lines (INT.Ov) were generated from solid primary or metastatic tumors as well as from ascitic fluid. Notably all lines expressed HLA class I, intercellular adhesion mol.-I (ICAM-I), polymorphic epithelial mucin (PEM), and cytokeratin (CK), but not HLA class II, B7.1 (CD80), or BAGE. While of the 9 lines tested 4 (INT.Ov1, 2, 5, and 6) expressed the folate receptor (FR-.alpha.) and 6 (INT.Ov1, 2, 5, 6, 7, and 9) expressed the epidermal growth factor receptor (EGFR); MAGE-I and p185HER-2/neu were only found in 2 lines (INT.Ov1 and 2) and GAGE-I expression in 1 line (INT.Ov2). The identification of class I MHC ligands and Tcell epitopes within protein antigens was achieved by applying several theor. methods including: (1) similarity or homol. searches to MHCPEP; (2) BIMAS; and (3) artificial neural network-based predictions of proteins MAGE, GAGE, EGFR, p185HER-2/neu, and FR-.alpha. expressed in INT.Ov lines. Because of the high frequency of expression of some of these proteins in ovarian cancer and the ability to det. HLA binding peptides efficiently, it is expected that after appropriate screening, a large cohort of ovarian cancer patients may become candidates to receive peptide-based vaccines.

ΙT 160212-35-1

RL: PRP (Properties)

(generation and phenotypic characterization of new human ovarian cancer cell lines with identification of antiqens potentially recognizable by HLA-restricted cytotoxic T cells)

ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:617992 HCAPLUS

DOCUMENT NUMBER: 127:277193

TITLE: Recombinant constructs encoding T

cell receptors specific for human

HLA-restricted tumor antigens INVENTOR(S): Sherman, Linda A.; Lustgarten, Joseph

Scripps Research Institute, USA

PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION: DD. W. D. V. O.

PAT	ENT NO.		KIND	DATE		APPLICATION NO.	DATE
WO	9732603 W: AU,			19970912		WO 1997-US3611	19970305
	RW: AT,	•	CH, DE		_		LU, MC, NL, PT, SE
	2246333 9721997			19970912 19970922		CA 1997-2246333 AU 1997-21997	19970305 19970305
EP	910409					EP 1997-914916	
	R: AT,		CH, DE,	, DK, ES,	FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,
JP PRIORITY	20005121 APPLN.		T2:	20000919			19970305 19960305

WO 1997-US3611 19970305

Methods are described to obtain nucleic acid mols. that encode T
cell receptors and their derivs. that are human HLA-restricted and
which are specific for tumor-assocd. antigens found in human tumors.
These nucleic acids are useful in prepg. recombinant cells for diagnosis
and therapy of human tumors. Demonstrated were selection of immunogenic
peptides of Her-2/neu: H3 and H7, induction of cytotoxic T
lymphocytes and lysis of human tumor by H3 and H7, and expression
of recombinant TCR derivs. specific for these peptides.

IT 160212-35-1

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(recombinant constructs encoding **T cell** receptors specific for human HLA-restricted tumor antigens)

L5 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1997:500233 HCAPLUS

DOCUMENT NUMBER:

127:117380

TITLE:

Immunostimulants comprising dendritic cell-binding protein fusion products with antigens and expression

vectors for disease treatment

INVENTOR(S):
PATENT ASSIGNEE(S):

Laus, Reiner; Ruegg, Curtis Landon; Wu, Hongyu Activated Cell Therapy, Inc., USA; Laus, Reiner;

Ruegg, Curtis Landon; Wu, Hongyu

SOURCE:

PRI

PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	CENT	NO.		KI	ND 	DATE			A	PPLI	CATI	N NC	DATE				
WO	WO 9724438			A1 19970710					W	0 19	96-U	19961223					
	W:	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,
		EE,	ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,
														NZ,			
														US,		-	-
		ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM					·	•	·	
	RW:	ΚE,	LS,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,
														CM,			
				SN,									-	•	•	•	,
US	6080	080409 A				2000	0627		US	3 199	95-5	7982	3	1995	L228		
CA	2241	373		A.	A	1997	0710		C.	A 19	96-22	2413	73	19961	L223		
ΑU	9713	380		A.	l	1997	0728		ΙA	J 199	97-13	3380		19961	L223		
ΑU	7167	83		B	2	2000	0309										
ΕP	8700	22		A.	1	1998	1014		E	2 19	96-94	14879	9	19961	L223		
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	FI											•			
JΡ	2000	5025	57	T	2	2000	0307		JI	9 19	97-52	24418	3	19961	L223		
US	5976	546		Α		1999	1102		US	199	98-14	16283	3	19980	903		
RITY	APP	LN.	INFO	.:					US	199	95-51	79823	3	19951	L228		
									Wo	199	96-US	32024	11	19961	1223		

AB Disclosed are therapeutic compns. and methods for inducing cytotoxic T cell responses in vitro and in vivo. The therapeutic compns. consist of antigen presenting cells activated by contact with a

fusion protein constructed by joining together a dendritic cell-binding protein and a polypeptide antigen. Also disclosed are expression vectors and systems for producing the polypeptide complexes. Examples include tumor prostatic acid phosphatase fusion products with GM-CSF, GM-CSF fusion products with oncogene antigen Her2, and p53 fusion products with GM-CSF. Fusion proteins were recombinantly expressed in either mammalian 293 cells or insect SF21 cells.

IT 192589-07-4P

> RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (amino acid sequence; immunostimulants comprising dendritic cell-binding protein fusion products with antigens and expression vectors for disease treatment)

ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2000 ACS L5

1997:455918 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 127:134444

TITLE: Conversion of in vitro cultured human monocytes into

effective presenters of an HER2/neu-encoded CTL

peptide epitope

AUTHOR (S): Wasserman, K.; Corsi, M. M.; Szekely, L.; Kono, K.;

Maes, H. H.; Kiessling, R.

CORPORATE SOURCE: Division of Basic Sciences, Laboratory of Experimental

Immunology, NCI-FCRDC, Frederick, MD, 21702-1201, USA

SOURCE: Scand. J. Immunol. (1997), 45(6), 678-682

CODEN: SJIMAX; ISSN: 0300-9475

PUBLISHER: Blackwell DOCUMENT TYPE: Journal LANGUAGE: English

AΒ Tumor-derived peptides have been surveyed, in a variety of systems, for their ability to elicit cytokine release from class I restricted T cells. Analogous studies on ovarian carcinoma have employed the antigen-processing defective T2 cell line. Purified dendritic cells (DC) have been reported to act as highly effective APC. A facile method was developed whereby DC-like cells were generated from monocyte precursors. Herein, evidence is presented suggesting DC-like cells are superior to T2 with respect to their ability to present a defined CTL epitope assocd. with ovarian carcinoma.

IT 160212-35-1

> RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(conversion of cultured human monocytes into effective presenters of HER2/neu-encoded cytotoxic T lymphocyte peptide epitope assocd. with ovarian carcinoma)

ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2000 ACS

1997:255985 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 126:316078

Identification of Her-2/Neu CTL epitopes using double TITLE:

transgenic mice expressing HLA-A2.1 and human CD.8

Lustgarten, Joseph; Theobald, Matthias; Labadie, AUTHOR (S):

Colleen; Laface, Drake; Peterson, Per; Disis, Mary L.;

Cheever, Martin A.; Sherman, Linda A.

CORPORATE SOURCE:

Department of Immunology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Hum. Immunol. (1997), 52(2), 109-118

> M. Smith 308-3278

CODEN: HUIMDQ; ISSN: 0198-8859

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

The Her-2/neu protooncogene is assocd. with malignant transformation and aggressive disease. Because of its overexpression in tumor cells and because it has been shown to be immunogenic, this protein represents an excellent target for T-cell immunotherapy. By identifying potential HLA-A2.1-binding peptides from the Her-2/neu sequence, peptides were selected as candidate T-cell epitopes. The immunogenicity of each peptide was evaluated by priming double transgenic mice expressing both the human (hu) CD8 and HLA-A2.1 mols. with synthetic peptides corresponding to these sequences. Because of the lack of interaction between murine CD8 and HLA-A2.1, expression of huCD8 on murine cells facilitates recognition of HLA mols. on human tumor cell lines. This led to the identification of two peptides that elicit an A2-restricted CTL response, one of which has not been previously identified. Both peptide-specific CTL populations were able to specifically lyse A2.1 and Her-2/neu expressing human tumor cells originating from a variety of tissues, demonstrating the utility of this murine model in identifying peptides presented by human cells. However, several Her-2/neu peptides previously reported to be immunogenic for human CTL were found not to be immunogenic in transgenic mice. The basis for these discrepancies is discussed.

IT 160212-35-1

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)

(identification of Her-2/Neu cytotoxic **T lymphocyte** epitopes using double transgenic mice expressing HLA-A2.1 and human CD8)

L5 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:485791 HCAPLUS

DOCUMENT NUMBER: 125:132739

TITLE: In vivo activation of tumor-specific cytotoxic

T cells

INVENTOR(S): Sherman, Linda A.

PATENT ASSIGNEE(S): Scripps Research Institute, USA

SOURCE: PCT Int. Appl., 157 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE		APPLICATION NO. DATE								
WO 9618409	Al 1996	0620	WO 1995-US16415	5 19951214							
W: AM, AT	, AU, BB, BG,	BR, BY, CA	, CH, CN, CZ, I	DE, DK, EE, ES, FI,							
GB, GE	, HU, IS, JP,	KE, KG, KP	, KR, KZ, LK, I	LR, LT, LU, LV, MD,							
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NE, SN	, TD, TG										
CA 2207736	AA 1996	0620	CA 1995-2207736 19951214								

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AU 9646007
                       A1
                            19960703
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                                                             19951214
     AU 712441
                       B2
                            19991104
     EP 793501
                       A1
                            19970910
                                           EP 1995-944127
                                                             19951214
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
     FI 9702514
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                            19970812
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                                                             19970613
     NO 9702729
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                                           NO 1997-2729
                                                             19970613
PRIORITY APPLN. INFO.:
                                           US 1994-355558
                                                             19941214
                                           WO 1995-US16415
                                                             19951214
     The present invention relates to methods, compns., and peptides useful in
AB
     activating CTLs in vivo with specificity for particular antigenic
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peptides. The invention also discloses the use of activated CTLs in vivo for the diagnosis and treatment of a variety of disease conditions, and compns. appropriate for these uses. Diagnostic systems, components, and methods are also described herein.

IT 160212-35-1P

> RL: BAC (Biological activity or effector, except adverse); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(peptides for in vivo activation of tumor-specific cytotoxic T cells)

ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2000 ACS

1996:235704 HCAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 124:314868

TITLE: Changes in an HER-2 peptide upregulating HLA-A2

> expression affect both conformational epitopes and CTL recognition: Implications for optimization of antigen

presentation and tumor-specific CTL induction

Fisk, Bryan; Savary, Cherylyn; Hudson, J. Michael; AUTHOR (S):

O'Brian, Catherine A.; Murray, James L.; Wharton, J.

Taylor; Ioannides, Constantin G.

CORPORATE SOURCE: Departments Gynecologic Oncology, University Texas,

Houston, TX, 77030, USA

SOURCE: J. Immunother. Emphasis Tumor Immunol. (1995), 18(4),

197-209

CODEN: JIEIEZ; ISSN: 1067-5582

DOCUMENT TYPE: Journal LANGUAGE: English

The HER-2/neu protooncogene (HER-2) is overexpressed in a significant no. AΒ of breast and ovarian tumors. Peptides of HER-2 sequence were recently found to reconstitute recognition of cytotoxic T lymphocytes (CTLs) from tumor-assocd. (TALs) and tumor-infiltrating (TILs) lymphocytes, indicating that they reconstitute

natural epitopes recognized by CTLs on HLA-A2+ tumors. Because HER-2 is an important antigen (Ag) for tumor-specific CTL induction and the immunogenicity of peptides for CTL induction is dependent on their presentation as stable complexes with HLA-A2, the authors identified peptides of high and low stabilizing activity from the sequence of HER-2 and the folate-binding protein (FBP). Distinct sequence patterns in the region positions (P) 3-P5 and P1 were found for peptides with high (HSA) and low (LSA) stabilizing ability. A low-HLA-A-A2-affinity HER-2 peptide, Pl of the CTL epitope, was permissive to substitutions that enhanced HLA-A2-stabilizing ability and conserved CTL recognition. In contrast, the region P3-P5 was not permissive to sequence changes. The selective permissivity of P1 and P9 in the tumor epitope sequence may have important implications for optimization of tumor Ag presentation, and

"neoantigenicity" of self-antigens, aiming toward induction of tumor-reactive CTLs of defined affinity and specificity for target Ags.

IT 160212-35-1

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(changes in HER-2 and folate-binding protein peptides upregulating HLA-A2 expression affect antigen presentation and tumor-specific cytotoxic T lymphocyte induction)

L5 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1995:590068 HCAPLUS

DOCUMENT NUMBER: 123:7736

TITLE: Identification of an immunodominant peptide of

HER-2/neu protooncogene recognized by ovarian

tumor-specific cytotoxic T

lymphocyte lines

AUTHOR(S): Fisk, Bryan; Blevins, Tracy L.; Wharton, J. Taylor;

Ioannides, Constantin G.

CORPORATE SOURCE: M.D. Anderson Cancer Center, Univ. Texas, Houston, TX,

77030, USA

SOURCE: J. Exp. Med. (1995), 181(6), 2109-17

CODEN: JEMEAV; ISSN: 0022-1007

DOCUMENT TYPE: Journal LANGUAGE: English

Synthetic peptide analogs of sequences in the HER-2 protooncogene (HER-2) were selected based on the presence of HLA-A2.1 anchor motifs to identify the epitopes on HER-2 recognized by ovarian tumor-reactive CTL. 19 Synthetic peptides were evaluated for recognition by four HLA-A2+ ovarian-specific cytotoxic T lymphocyte (CTL) line obtained from leukocytes assocd. with ovarian tumors. The nonapeptide E75 (HER-2, 369-377:KIFGSLAFL) was efficient in sensitizing T2 cells for lysis by all four CTL lines. This peptide was specifically recognized by cloned CD8+ CTL isolated from one of the ovarian-specific CTL lines. E75-pulsed T2 cells inhibited lysis by the same CTL clone of both an HLA-A2+ HER-2high ovarian tumor and a HER-2high cloned ovarian tumor line transfected with HLA-A2, suggesting that this or a structurally similar epitope may be specifically recognized by these CTL on ovarian tumors. Several other HER-2 peptides were recognized preferentially by one or two CTL lines, suggesting that both common and private HER-2 epitopes may be immunogenic in patients with ovarian tumors. Since HER-2 is a self-antigen, these peptides may be useful for understanding mechanisms of tumor recognition by T cells, immunol. tolerance to tumor, and structural characterization of tumor antigens.

IT 160212-35-1

RL: PRP (Properties)

(identification of an immunodominant peptide of HER-2/new protooncogene recognized by ovarian tumor-specific cytotoxic \mathbf{T}

lymphocyte lines)

L5 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2000 ACS ACCESSION NUMBER: 1995:294003 HCAPLUS

DOCUMENT NUMBER: 122:263516

TITLE: HLA-A2.1 binding peptides and their detection and uses

INVENTOR(S): Grey, Howard M.; Sette, Alessandro; Sidney, John;

Kast, W. Martin

PATENT ASSIGNEE(S): Cytel Corp., USA

09/277,074 Davis

SOURCE: PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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										AU 1994-63594									
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E	3R	9406	652		A		1996	0910		B	R 19	94-6	652		1994	0304			
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PRIORI	TY	APP	LN.	INFO	. :					U	s 19	93-2	7146		1993	0305			
										U	s 19	93-7	3205		1993	0604			
										U	s 19	93-1	5918	4	1993	1129			
										W	O 19	94-U	S235	3	1994	0304			

An algorithm for selecting immunogenic oligopeptides capable of AΒ specifically binding glycoproteins encoded by HLA-A2.1 allele and inducing T cell activation in T cells

restricted by the A2.1 allele. The peptides are useful to elicit an immune response against a target antigen. Identification of immunogenic oligopeptides from viral or tumor-related proteins was demonstrated.

IT 160212-35-1

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (HLA-A2.1-binding immunogenic peptide and algorithm for its identification)

ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2000 ACS L5

1995:60411 HCAPLUS ACCESSION NUMBER:

122:206764 DOCUMENT NUMBER:

An expression profile of active genes in human colonic TITLE:

mucosa

Okubo, Kousaku; Yoshii, Junji; Yokouchi, Hideoki; AUTHOR (S):

Kameyama, Masao; Matsubara, Kenichi

Ins. Mol. Cell. Biol., Osaka Univ., Suita, 565, Japan CORPORATE SOURCE:

DNA Res. (1994), 1(1), 37-45 SOURCE:

CODEN: DARSE8; ISSN: 1340-2838

DOCUMENT TYPE: Journal English LANGUAGE:

An expression profile of genes active in the human colonic mucosa was obtained by collecting 959 partial sequences from a 3'-directed cDNA library. Seven genes were found to produce mRNA each of which comprised more than 1% of total mRNA. Four of these genes are novel, and are likely to be uniquely expressed in the colonic mucosa, and the other three have

been identified as genes for fatty acid binding protein, Ig lambda chain, and carcinoma-assocd. antigen GA733-2. In the remaining 952 clones, 310 were composed of 118 species occurred recurrently but less than 1%, and 533 clones appeared only once. Because the 3'-directed cDNA library faithfully represents the mRNA population in the source tissue, these nos. represent the relative activities of the gene expression. Altogether 156 gene species were identified in GenBank, and a significant portion of these genes encode proteins found in Golgi app. and lysosomes, chromosome-encoded mitochondrial proteins, cell surface proteins, and components in the protein synthesis machinery. The types and proportions of genes identified is consistent with the known major activities of the colonic mucosa such as mucous protein prodn., energy-dependent water absorption, and rapid cell proliferation and turnover.

IT 100630-38-4, Receptor (human MKN-7 cell gene c-erbB2 precursor
 protein moiety reduced)

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(amino acid sequence of; expression profile of active genes in human colonic mucosa)

=> select hit rn 15 1-24

E1 THROUGH E7 ASSIGNED

=> fil reg

FILE 'REGISTRY' ENTERED AT 15:41:38 ON 15 NOV 2000 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES: 14 NOV 2000 HIGHEST RN 302896-64-6 DICTIONARY FILE UPDATES: 14 NOV 2000 HIGHEST RN 302896-64-6

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

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                 (264622-09-5/RN)
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L6
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               AND L1
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L6
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RN
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     Glycine, L-lysyl-L-isoleucyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-
     alanyl-L-phenylalanyl-L-leucyl-L-prolyl-L-.alpha.-glutamyl-L-seryl-L-
     phenylalanyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
     18: PN: WO0020027 SEQID: 4 claimed protein
CN
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     Human Her2 protein (369-383)
LC
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SOL
    15
     264622-09-5 REGISTRY
RN
SEO
         1 KIFGSLAFLP ESFDG
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L6
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    Neu (receptor) (human) (9CI) (CA INDEX NAME)
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OTHER NAMES:
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SEQ
       351 REVRAVTSAN IQEFAGCKKI FGSLAFLPES FDGDPASNTA PLQPEQLQVF
                              == ======
HITS AT:
          369-377
REFERENCE 1: 132:292701
    ANSWER 3 OF 7 REGISTRY COPYRIGHT 2000 ACS
1.6
    258494-99-4 REGISTRY
RN
     Immunoglobulin (mouse clone DC8scFv/erbB2EC single-chain precursor) fusion
CN
     protein with peptide (synthetic human p53 (protein) tetramerization)
     fusion protein with neu (receptor) (human fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
     35: PN: WO0006605 FIG: 49 claimed protein
CN
LC
    STN Files:
                CA, CAPLUS
SOL 951
RN
    258494-99-4 REGISTRY
SEO
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                                   M. Smith
                                              308-3278
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Page 23

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HITS AT: 660-668

REFERENCE 1: 132:165123

L6 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2000 ACS

RN 204380-34-7 REGISTRY

CN L-Aspartic acid, L-lysyl-L-isoleucyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-phenylalanyl-L-leucyl-L-prolyl-L-.alpha.-glutamyl-L-seryl-L-phenylalanyl-L-.alpha.-aspartylglycyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

SQL 16

RN 204380-34-7 REGISTRY

SEO 1 KIFGSLAFLP ESFDGD

========

HITS AT: 1-9

REFERENCE 1: 128:213387

L6 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2000 ACS

RN 192589-07-4 REGISTRY

CN Phosphatase, acid (rat) fusion protein with colony-stimulating factor 2

(rat) (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

SOL 782

RN 192589-07-4 REGISTRY

SEQ 351 REVRAVTSAN IQEFAGCKKI FGSLAFLPES FDGDPASNTA PLQPEQLQVF

== ======

HITS AT: 369-377

REFERENCE 1: 127:117380

L6 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2000 ACS

RN 160212-35-1 REGISTRY

CN L-Leucine, L-lysyl-L-isoleucyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-

alanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Leucine, N-[N-[N-[N-[N-[N-[N-(N-L-lysyl-L-isoleucyl)-L-

phenylalanyl]glycyl]-L-seryl]-L-leucyl]-L-alanyl]-L-phenylalanyl]-

OTHER NAMES:

CN 29: PN: WO0034494 TABLE: 1 claimed protein

CN 31: PN: WO0053161 SEQID: 70 unclaimed sequence

CN 40: PN: WO0049041 SEQID: 44 claimed sequence

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

SOL 9

RN 160212-35-1 REGISTRY

SEQ 1 KIFGSLAFL

HITS AT: 1-9

REFERENCE 1: 133:256752

REFERENCE 2: 133:191988

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3: 133:54574
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           9: 129:229561
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     ANSWER 7 OF 7 REGISTRY COPYRIGHT 2000 ACS
L6
     100630-38-4 REGISTRY
RN
CN
     Receptor (human MKN-7 cell gene c-erbB2 precursor protein moiety reduced)
     (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (1-633)-(650-1255)-Neu (receptor) (human)
    1: PN: WO0044899 SEQID: 1 unclaimed protein
2: PN: WO0020579 SEQID: 2 claimed protein
2: PN: WO9957981 SEQID: 5 unclaimed protein
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CN
CN
     GenBank X03363-derived protein
CN
CN
     Receptor (human gene c-erbB2 precursor)
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CN
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REFERENCE 7: 104:103428